ornithine transcarbamylase deficiency

Ornithine transcarbamylase deficiency is an inherited disorder that causes ammonia to accumulate in the blood. Ammonia, which is formed when proteins are broken down in the body, is toxic if the levels become too high. The nervous system is especially sensitive to the effects of excess ammonia.

Ornithine transcarbamylase deficiency often becomes evident in the first few days of life. This severe, early-onset form of the disorder usually affects males; it is very rare in females. An infant with ornithine transcarbamylase deficiency may be lacking in energy (lethargic) or unwilling to eat, and have a poorly-controlled breathing rate or body temperature. Some babies with this disorder may experience unusual body movements, seizures, or coma. Complications from ornithine transcarbamylase deficiency may include developmental delay and intellectual disability. Progressive liver damage, skin lesions, and brittle hair may also occur.

In some affected individuals, signs and symptoms of ornithine transcarbamylase deficiency may be less severe, and may not appear until later in life. The later-onset form of the disorder occurs in both males and females. People with later-onset ornithine transcarbamylase deficiency may experience episodes of altered mental status, such as delirium, erratic behavior, or a reduced level of consciousness. Headaches, vomiting, aversion to protein foods, and seizures can also occur in this form of the disorder.

Frequency

Estimates of the prevalence of ornithine transcarbamylase deficiency have ranged from 1 in 14,000 to 1 in 77,000 people. Individuals with the early-onset form of the disorder are more likely to be counted in these estimates, because people with the later-onset form are less likely to come to medical attention.

Genetic Changes

Mutations in the *OTC* gene cause ornithine transcarbamylase deficiency. The *OTC* gene provides instructions for making the ornithine transcarbamylase enzyme.

Ornithine transcarbamylase deficiency belongs to a class of genetic diseases called urea cycle disorders. The urea cycle is a sequence of reactions that occurs in liver cells. It processes excess nitrogen, generated when protein is used by the body, to make a compound called urea that is excreted by the kidneys. The ornithine transcarbamylase enzyme starts a specific reaction within the urea cycle.

In ornithine transcarbamylase deficiency, as its name suggests, the ornithine transcarbamylase enzyme is damaged or missing. The urea cycle cannot proceed normally, and nitrogen accumulates in the bloodstream in the form of ammonia.

Ammonia is especially damaging to the nervous system, so ornithine transcarbamylase deficiency causes neurological problems as well as eventual damage to the liver.

Inheritance Pattern

Ornithine transcarbamylase deficiency is an X-linked disorder. A condition is considered X-linked if the mutated gene that causes the disorder is located on the X chromosome, one of the two sex chromosomes. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

In males (who have only one X chromosome), one altered copy of the gene in each cell is sufficient to cause the condition. In females (who have two X chromosomes), mutations in both copies of the gene will cause the disorder. Some females with only one altered copy of the *OTC* gene also show signs and symptoms of ornithine transcarbamylase deficiency.

Other Names for This Condition

- Ornithine Carbamoyltransferase Deficiency Disease

Diagnosis & Management

Formal Treatment/Management Guidelines

- American College of Medical Genetics: Ornithine Transcarbamylase Deficiency Transition to Adult Health Care ACT Sheet
  https://www.acmg.net/StaticContent/ACT/OTC_Deficiency_Transition.pdf
- New England Consortium of Metabolic Programs: Acute Illness Protocol
  http://newenglandconsortium.org/for-professionals/acute-illness-protocols/urea-cycle-disorders/ornithine-transcarbamylase-deficiency-otc/

Genetic Testing

- Genetic Testing Registry: Ornithine carbamoyltransferase deficiency
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268542/

Other Diagnosis and Management Resources

- Baby's First Test
  http://www.babysfirsttest.org/newborn-screening/conditions/ornithine-transcarbamylase-deficiency
- GeneReview: Ornithine Transcarbamylase Deficiency
  https://www.ncbi.nlm.nih.gov/books/NBK154378

- GeneReview: Urea Cycle Disorders Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1217
- MedlinePlus Encyclopedia: Hereditary urea cycle abnormality
  https://medlineplus.gov/ency/article/000372.htm
- National Organization for Rare Disorders (NORD) Physician Guide: Urea Cycle Disorders
  http://nordphysicianguides.org/urea-cycle-disorders/

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Hereditary urea cycle abnormality
  https://medlineplus.gov/ency/article/000372.htm
- Health Topic: Genetic Brain Disorders
  https://medlineplus.gov/geneticbraindisorders.html
- Health Topic: Metabolic Disorders
  https://medlineplus.gov/metabolicdisorders.html
- Health Topic: Newborn Screening
  https://medlineplus.gov/newbornscreening.html

Genetic and Rare Diseases Information Center

- Ornithine transcarbamylase deficiency
  https://rarediseases.info.nih.gov/diseases/8391/ornithine-transcarbamylase-deficiency

Educational Resources

- Disease InfoSearch: Ornithine transcarbamylase deficiency
  http://www.diseaseinfosearch.org/Ornithine+transcarbamylase+deficiency/5412
- Genetics Education Materials for School Success (GEMSS)
  http://www.gemssforschools.org/conditions/urea-cycle/default
- MalaCards: ornithine transcarbamylase deficiency
  http://www.malacards.org/card/ornithine_transcarbamylase_deficiency
- Orphanet: Ornithine transcarbamylase deficiency
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=664

Patient Support and Advocacy Resources

- Children Living with Inherited Metabolic Diseases
  http://www.climb.org.uk/
- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/ornithine-transcarbamylase-deficiency/
- National Urea Cycle Disorders Foundation
  http://nucdf.org
- Urea Cycle Disorders Consortium
  http://www.rarediseasesnetwork.org/cms/UCDC

GeneReviews

- Ornithine Transcarbamylase Deficiency
  https://www.ncbi.nlm.nih.gov/books/NBK154378
- Urea Cycle Disorders Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1217

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22ornithine+transcarbamylase+deficiency%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Ornithine+Carbamoyltransferase+Deficiency+Disease%5BMAJR%5D%29+AND+%28ornithine+transcarbamylase+deficiency%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- ORNITHINE TRANSCARBAMYLASE DEFICIENCY, HYPERAMMONEMIA DUE TO
  http://omim.org/entry/311250

Sources for This Summary

- Brassier A, Gobin S, Arnoux JB, Valayannopoulos V, Habarou F, Kossorotoff M, Servais A, Barbier V, Dubois S, Touati G, Barouki R, Lesage F, Dupic L, Bonnefont JP, Ottolenghi C, De Lonlay P. Long-term outcomes in Ornithine Transcarbamylase deficiency: a series of 90 patients. Orphanet J Rare Dis. 2015 May 10;10:58. doi: 10.1186/s13023-015-0266-1.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/25958381
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4443534/
- Caldovic L, Abdikarim I, Narain S, Tuchman M, Morizono H. Genotype-Phenotype Correlations in Ornithine Transcarbamylase Deficiency: A Mutation Update. J Genet Genomics. 2015 May 20; 42(5):181-94. doi: 10.1016/j.jgg.2015.04.003. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/26059767
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4565140/
- Choi JH, Lee BH, Kim JH, Kim GH, Kim YM, Cho J, Cheon CK, Ko JM, Lee JH, Yoo HW. Clinical outcomes and the mutation spectrum of the OTC gene in patients with ornithine transcarbamylase deficiency. J Hum Genet. 2015 Sep;60(9):501-7.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/25994866
- GeneReview: Urea Cycle Disorders Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1217
- Helman G, Pacheco-Colón I, Gropman AL. The urea cycle disorders. Semin Neurol. 2014 Jul;34(3): 341-9. doi: 10.1055/s-0034-1386771.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/25192511
- OMIM: ORNITHINE TRANSCARBAMYLASE DEFICIENCY, HYPERAMMONEMIA DUE TO
  http://omim.org/entry/311250

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